



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/662,713

09/15/2003

Perry D. Haaland

P-5768

1008

64154

7590

08/06/2009

David W. Highet, VP & Chief IP Counsel
Becton, Dickinson and Company
(Antonelli, Terry, Stout & Krause, LLP)
1 Becton Drive, MC 110
Franklin Lakes, NJ 07417-1880

EXAMINER

RIGGS II, LARRY D

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

08/06/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/662,713	Applicant(s) HAALAND ET AL.	
	Examiner LARRY D. RIGGS II	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

In view of the appeal brief filed on 20 April 2009, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Status of Claims

Claims 1-36 are currently pending and under consideration.

Withdrawn Rejections/Objections

The rejection of claims 1-20 under 35 U.S.C. §102(b) over Akong et al., in the Office action mailed 19 August 2008 is withdrawn in view of the arguments filed 20 April 2009.

The rejection of claims 1 and 6-8 under 35 U.S.C. §103(a) over Akong et al. in view of Eggers et al., in the Office action mailed 19 August 2008 is withdrawn in view of the arguments filed 20 April 2009.

The rejection of claims 1, 13 and 14 under 35 U.S.C. §103(a) over Akong et al. in view of Eggers et al. and further in view of Ali et al., in the Office action mailed 19 August 2008 is withdrawn in view of the arguments filed 20 April 2009.

The rejection of claims 1 and 25-29 under 35 U.S.C. §103(a) over Akong et al. in view of Eggers et al. and further in view of Fink et al., in the Office action mailed 19 August 2008 is withdrawn in view of the arguments filed 20 April 2009.

The rejection of claims 1, 30 and 31 under 35 U.S.C. §103(a) over Akong et al. in view of Eggers et al. and further in view of Terramani et al., in the Office action mailed 19 August 2008 is withdrawn in view of the arguments filed 20 April 2009.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

This objection is maintained and reiterated from the previous office action, mailed 19 August 2009.

Claims 6 and 12 are objected to because of the following informalities:

Claim 6 provides "said receptacles includes" in line 1. It is suggested that applicant replace "includes" with "include" to result in grammatical correctness.

Claim 12 provides "in order determine" in line 3. It is suggested that applicant replace the phrase with "in order to determine" to result in grammatical correctness. Appropriate correction is required.

Specification

The uses of the trademarks such as MATLAB, MATHEMATICA, S-PLUS, META MORPH, DISCOVERY -1, WINDOWS 2000, BIOMEK-FX, BIOMEK 2000, TECAN GENISIS, etc. have been noted in this application. They can be found, for example, paragraph 40 of the amended specification filed 28 March 2008; paragraphs 41, 42, 80, 81, etc. of the specification, filed 15 September 2003. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Trademarks should be identified by capitalizing each letter of the mark (in the case of word or letter marks) or otherwise indicating the description of the mark (in the case of marks in the form of a symbol or device or other nontextual form). See MPEP 608.01(v).

The software programs MATLAB, MATHEMATICA, S-PLUS, META MORPH and WINDOWS 2000 provided in paragraphs 40 and 41 are not capitalized (in the case of word or letter marks). The platform software programs BIOMEK-FX, BIOMEK 2000, TECAN GENISIS are not capitalized, (see paragraph 42). The name of the fluorescent

Art Unit: 1631

microscope DISCOVERY -1 was not capitalized, (see paragraph 80). The software program META MORPH was not capitalized, (see paragraph 81).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-30 are rejected because they depend from claim 1.

Claim 1 provides “contacting said placed mixtures with said cells” in line 14. There is no antecedent basis for the limitation because there are no “cells” provided previously in the instant claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Art Unit: 1631

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant rejection is newly applied with current art and new art of record.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima et al., (US 5,906,828), in view of Sherrill et al. (J. Assoc. Laboratory Automation, 1999, 4(6), 76-84) and further in view of Greco et al., (Pharmacological Rev., 1995, 47(2):33 1-385).

The instant claims provide a method for identifying agents that cause a phenotypic change in a cell comprising: providing receptacles in an array, providing a statistical design including generic names, factor levels and experimental runs, utilizing software to map agents, concentrations and locations to an array, placing different mixtures of agents into receptacles by experimental design, contacting cells with the mixtures, acquiring data, utilizing an algorithm for comparing the data with the statistical

Art Unit: 1631

design to identify which agents are effective in causing a phenotypic change in the cells and storing the experimental design, agent identities and acquired data in a database.

Regarding claim 1, Cima et al. discloses a method for screening compounds for effects on cell growth, proliferation, metabolism, and DNA synthesis (coil 10, lines 50-58). Cima et al. discloses immobilizing mixtures of agents on a solid support (col. 2, line 55 through col. 3, line 5; col. 6, lines 24-38; col. 7, lines 37-45; col. 7, lines 8-35; Col. 8, line 66 through col. 9, line 3; claim 1). Cima et al. discloses growth effector molecules as being immobilized agents (col. 6, lines 24-38). Cima et al. discloses contacting mixtures of agents with a whole cell (col. 13, lines 38-56; claim 1). Cima et al. discloses acquiring desired biological response and identifying mixtures of agents having an effect in producing a desired biological effect (col. 3, lines 2-5; col. 6, lines 24-38; col. 9, lines 12-17; col. 10, lines 50-58; example 1).

Although Cima et al. discloses using a membrane and a 96-well manifold apparatus for dotblot assay, Cima et al. does not specifically disclose using receptacles for placing agent mixtures. Cima et al. does not disclose statistical design and software for obtaining different mixtures of agents, using an algorithm for identifying an effective agent or storing the statistical design and resulting data.

Sherrill et al. provides a method of developing statistical experimental design and liquid handling for assays by providing receptacles in an array, statistical design with general factor names, factor levels and experimental runs, (page 76, left column, fourth paragraph – page 78, left column, third paragraph; page 78, right column; Table 1; Figures 3 and 5). Sherrill et al. shows storing the statistical design and resulting

Art Unit: 1631

experimental data, (page 79, left column, last paragraph; page 83, right column, first paragraph).

Cima et al. and Sherrill et al. do not show utilizing an algorithm for identifying an effective agent.

Greco et al. discloses using a statistical design (p. 373-376) and statistical models (fig. 1, text on p. 334-335) for assessing synergistic effect (i.e., biological response) of mixtures of agents (see, for example, p. 360, left column, p. 376, right col. and table 3 on p. 350). Greco et al. shows an algorithm for comparing acquired data with the statistical design, (page 362, left column; page 375, right column, second paragraph – page 376, left column, third paragraph).

Regarding claim 2, Sherrill et al. shows user inputs of identities, amounts of agents with the SAGIAN AAO software, (page 78, right column, #3; page 82, left column; Figures 3 and 5).

Regarding claim 3, Sherrill et al. shows user inputs of statistical design, (page 76, right column, last paragraph – page 77, right column, third paragraph; page 79, left column; page 81, left column).

Regarding claim 4, Sherrill et al. shows automated functions provided by the programmed software, including robotics (page 78, right column, first paragraph; page 81, right column, third and fourth paragraphs; page 82, right column).

Regarding claim 5, Sherrill et al. shows either pipetting agents into experiment wells or preparing intermediate buffer mixtures and then pipetting aliquots of pre-mixed solutions into experiment wells, (page 82, left column, first paragraph).

Art Unit: 1631

Regarding claims 6-8, Cima et al. discloses immobilizing mixtures of agents on a solid support (col. 2, line 55 through col. 3, line 5; col. 6, lines 24-38; col. 7, lines 37-45; col. 7, lines 8-35; Col. 8, line 66 through col. 9, line 3; claim 1). Cima et al. discloses growth effector molecules as being immobilized agents (col. 6, lines 24-38). Cima et al. discloses coating with an agent immobilized material wherein the material may contain groups for covalent immobilization of an agent (col. 5-6, Section Attachment Substrates and col. 7, Attachment Methods). Cima et al. discloses optionally using a coating which enhances the attachment of cells to a surface (col. 6, lines 16- 22).

Regarding claim 9, Sherrill et al. shows that designs, protocols, maps and assay data are stored, indicating that the data is “integrated” or stored together in one place, (page 79, left column, last paragraph; page 83, right column, first paragraph).

Regarding claim 10, Greco et al. shows fitting statistical models to experimental data, (page 335, right column, first and second paragraphs; page 376, right column, second paragraph).

Regarding claim 11, Sherrill et al. shows directly comparing controls and mixtures, (Figure 6).

Regarding claim 12, Sherrill et al. shows multiple experiments depending on the user's desire to determine resolution of factor interaction, (page 77, right column, third paragraph - page 78, left column; Figure 2; Table 2). Sherrill et al. shows updating storing of information, and data, because of previously stored information or recently created information, may be utilized (page 79, left column).

Art Unit: 1631

Greco et al. shows models for pattern or cluster analysis, (page 371, right column, second paragraph).

Regarding claim 13, Greco et al. shows d-optimal design, (page 375, right column).

Regarding claim 14, Sherrill et al. shows statistical space filling design based on experimental coverage, (page 77, right column, second paragraph; page 80, right column, fourth-sixth paragraphs; Figures 3 and 5).

Regarding claims 15 and 16, Cima et al. screening compounds for effects on cell growth, proliferation, metabolism, and DNA synthesis (col 10, lines 50-58). Cima discloses growth effector molecules as being immobilized agents (column 4, lines 2-10; col. 6, lines 24-38).

Regarding claims 17 and 18, Greco et al. shows refining a design of a combination experiment based on data of the larger previous experiment and repeating, (page 375, left column, second paragraph). Sherrill et al. shows subsets of wells and variation of concentrations depending on the design, (page 82, left column; Figure 5).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Cima et al. to use receptacles for placing agents, such as taught by Sherrill et al., where the motivation would have been to use a experimental design and integrated liquid handling to create more robust, cost-effective assays, as taught by Sherrill et al., (page 76, left column, second paragraph). It would also have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Cima et al. and Sherrill et al. to use statistical models

Art Unit: 1631

for identifying agents producing a desired biological response, such as taught by Greco, where the motivation would have been to assess combination of agents that yield an unexpected enhanced pharmacological effect and the nature and intensity of drug interaction, as taught by Greco, (page 333, middle of right column; page 334, top of right column).

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima et al., (US 5,906,828), in view of Sherrill et al. (J. Assoc. Laboratory Automation, 1999, 4(6), 76-84) in view of Greco et al., (Pharmacological Rev., 1995, 47(2):33 1-385) as applied to claims 1-18 above, and further in view of Thastrup et al. (US 6,518,021).

The instant claims 19-24 depends from claim 1 with the extra limitations of identifying internal cellular mechanisms (claim 19) by extracting scientific information on cellular pathways and comparing the information with the identified agents and phenotypic change (claim 20) extracted by a computer (claim 21), wherein extracted information comprises a plurality of data types (claim 22) or by identifying genes and/or proteins expressed in the cells in the presence of the agents (claim 23) or by identifying which receptors on the cells are activated in the presence of the agents (claim 24).

Cima et al. in view of Sherrill et al. in view of Greco et al. is applied to 1-18 above.

Cima et al. in view of Sherrill et al. in view of Greco et al. do not show identifying internal cellular mechanisms (claim 19) by extracting scientific information on cellular pathways and comparing the information with the identified agents and phenotypic

Art Unit: 1631

change (claim 20) extracted by a computer (claim 21), wherein extracted information comprises a plurality of data types (claim 22) or by identifying genes and/or proteins expressed in the cells in the presence of the agents (claim 23) or by identifying which receptors on the cells are activated in the presence of the agents (claim 24).

Regarding claims 19 and 20, Thastrup et al. shows a method of extracting quantitative information, i.e. which intracellular pathway is related to an influence on a cellular response when exposing cells to an agent or mixture of agents, (column 3, line 43 – column 4, line 29; column 5, lines 36 – 55; column 7, lines 16 – 22; column 8, line 56 – column 9, line 46).

Regarding claim 21, Thastrup et al. shows the preferred embodiment of the method automated with the computer acquiring, storing and computing the degree of redistribution of images (analysis), (column 6, line 38- column 7, line 22).

Regarding claim 22, Thastrup et al. shows data on multiple cellular pathways, (columns 24-35; Examples 3-22).

Regarding claim 23, Thastrup et al. shows proteins expressed, i.e. expressed fluorescent probe in transfected cells as a result of exposure to agents, (column 9, lines 27 – 46; column 10, line 59 – column 11, line 4; Example 3).

Regarding claim 24, Thastrup et al. shows identifying which receptors are activated when exposed to agents, (column 30, lines 50-58; column 31, lines 17-47).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Cima et al. in view of Sherrill et al. in view of Greco et al. with method of extracting information from a plurality of cells genetically

Art Unit: 1631

modified to provide cellular pathway information related to a cellular response when exposed to agents, as shown by Thastrup et al. where the motivation to combine is that the method by Thastrup et al. allows biologically active substances with completely novel modes of action to be identified in a way that insures very high selectivity to the particular isoform of the biologically active polypeptide and further development of compound selectivity versus other components of the same signaling pathway, (column 3, line 60 - column 4, line 5).

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima et al., (US 5,906,828), in view of Sherrill et al. (J. Assoc. Laboratory Automation, 1999, 4(6), 76-84) in view of Greco et al., (Pharmacological Rev., 1995, 47(2):33 1-385) in view of Thastrup et al. (US 6,518,021), as applied to claims 1-24 above, and further in view of Fink et al. (US, 5,808,918).

The instant claims 25-29 depends from claim 1 with the extra limitations of calculating the likelihood that a cellular pathway, protein or gene is involved in the phenotype associated with the agents using scientific information (claim 25), the scientific information is from a plurality of data types (claim 26) the information is stored on a database(s) (claim 27), the information comprises identifying genes and/or proteins expressed in the cells in the presence of the agents (claim 28) or by identifying which receptors on the cells are activated in the presence of the agents (claim 29).

Cima et al. in view of Sherrill et al. in view of Greco et al. in view of Thastrup et al. is applied to 1-24 above.

Cima et al. in view of Sherrill et al. in view of Greco et al. in view of Thastrup et al. do not show calculating the likelihood that a cellular pathway, protein or gene is involved in the phenotype associated with the agents using scientific information (claim 25), the scientific information is from a plurality of data types (claim 26) the information is stored on a database(s) (claim 27), the information comprises identifying genes and/or proteins expressed in the cells in the presence of the agents (claim 28) or by identifying which receptors on the cells are activated in the presence of the agents (claim 29).

Regarding claim 25, Fink et al. shows a method of using scientific information to provide a modeling system that provides insight into phenomena at the sub-cellular, cellular, organ, system or patient levels, (abstract; column 7, line 49 – column 8, line 7). Fink shows a utilizing the model with a collection of information regarding an impact of an agent, i.e. drug, on certain biological factors and providing a prediction of what will happen at certain biological levels. Fink shows a system that simulates interrelated biological findings and hypotheses at the cellular and subcellular levels to identify new drug targets, to develop a better understanding of key biological mechanisms, and to assess the potential for influencing important clinical outcomes, (column 3, lines 7-23; column 12, line 44 – column 13, line 13).

Regarding claims 26 and 28, Fink et al. shows utilizing experimental data, (column 7, lines 49-63). Thastrup et al. shows data on multiple cellular pathways, (columns 24-35; Examples 3-22), and proteins expressed, i.e. expressed fluorescent

Art Unit: 1631

probe in transfected cells as a result of exposure to a agents, (column 9, lines 27 – 46; column 10, line 59 – column 11, line 4; Example 3).

Regarding claim 27, Fink et al shows the scientific information is synthesized into the knowledge diagram, (column 7, lines 61-65).

Regarding claim 29, Thastrup et al. shows identifying which receptors are activated when exposed to agents, (column 30, lines 50-58; column 31, lines 17-47).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Cima et al. in view of Sherrill et al. in view of Greco et al. in view of Thastrup et al. with a modeling system, as shown by Fink et al., where the motivation to combine is that the modeling system by Fink et al. would allow one skilled in the art to develop a better understanding of key biological mechanisms, and to assess the potential for influencing important clinical outcomes, (column 3, lines 7-23).

Claims 1-18, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima et al., (US 5,906,828), in view of Sherrill et al. (J. Assoc. Laboratory Automation, 1999, 4(6), 76-84) in view of Greco et al., (Pharmacological Rev., 1995, 47(2):33 1-385) as applied to claims 1-18 above, and further in view of Terramani et al. (In Vitro Cell. Dev. Biol.; Human Macrovascular Endothelial Cells: Optimization of Culture Conditions, 2000, 36, 125-132).

The instant claims 30 and 31 depends from claim 1 with the extra limitations that the phenotypic data is acquired by immunocytochemistry analysis (claim 30) and the

Art Unit: 1631

analysis determines whether biological markers are present that indicate proliferation and/or differentiation of the cells in presence of the agents (claim 31).

Cima et al. in view of Sherrill et al. in view of Greco et al. is applied to 1-18 above.

Cima et al. in view of Sherrill et al. in view of Greco et al. do not show the phenotypic data is acquired by immunocytochemistry analysis (claim 30) and the analysis determines whether biological markers are present that indicate proliferation and/or differentiation of the cells in presence of the agents (claim 31).

Regarding claims 30 and 31, Terramani et al. provides a study to identify optimal culture conditions to support the proliferation of human macrovascular endothelial cells. Terramani, et al. shows data acquired by immunochemistry analysis indicating biological marker, vWF when staining HSVEC and HUVEC cells in their use of proliferation studies with cellular mitogens, (see page 126, left column, last full paragraph – right column, third paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method of Cima et al. in view of Sherrill et al. in view of Greco et al. with immunocytochemistry analysis as shown by Terramani et al. where the motivation to combine would be to better understand the cellular impact of the drug.

Claims 32-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima et al., (US 5,906,828), in view of Sherrill et al. (J. Assoc. Laboratory Automation, 1999, 4(6), 76-84) in view of Greco et al., (Pharmacological Rev., 1995, 47(2):33 1-

Art Unit: 1631

385), as applied to claims 1-18 above, and further in view of Biomek 2000, (Beckman Coulter, Inc., 1998, User's Guide, Part No. 609909-AA, 1-80).

The instant claim is drawn to a system for identifying agents that cause a phenotypic change in a cell comprising an array of receptacles, a statistical design of names factor levels and experimental runs, a software program for generating the statistical design and mapping of locations, concentrations and agents, acquiring experimental data, an algorithm for comparing the experimental data with the statistical design to identify which mixtures of agents causing a phenotypic change in the cells, a database for storing the statistical design, agents identities, experimental data and results of the comparison.

Cima et al., Sherrill et al. and Greco et al. are applied to claims 1-18. Cima et al., Sherrill et al. and Greco et al. show using software programs referred to as SAGIAN AUTOMATED ASSAY OPTIMIZATION (AAO), SILAS and the BIOMEK 2000 (Sherrill et al., page 76, left column, second and third paragraphs; page 80-81; Figures 3, 5 and 7), and likewise show receptacles, providing a statistical design, generating mapping and acquiring the experimental data, a database and imply the use of a processor to execute the above programs (see above). However, they do not show a system. Likewise they do not show robotic system limitations (claims 34 and 35).

Biomek 2000 is a robotic system that may be programmed for liquid handling, (pages 1-1, 1-2, Chapter 3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method of Cima et al. in view of Sherrill et al. in view of

Art Unit: 1631

Greco et al. with the User's Guide of the Biomek 2000 where the motivation to combine would be to provide a system that would allow the automation of the method of Cima et al. in view of Sherrill et al. in view of Greco et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims (1-3), 5, 6, (7-8), 16, 30 and 31 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11, and claims 2, 3, 4, 6-8 in view of claim 11, respectively, of copending Application No. 12/015,233.

Art Unit: 1631

Although the conflicting claims are not identical, they are not patentably distinct from each other because the recited limitations of the claims are exact except for the use of a program to experimentally design a mixture of agents and identifying mixtures of effective agents, as recited in the instant claims. Likewise, the algorithm of copending claim 11 makes the use of a computer obvious.

Clearly, claim 11 of the copending application teaches identifying which mixtures of single agents are effective in producing a desired biological response in contacted cells using a statistical design, and thus anticipates the instant claim 1. Claims 5-8, 16, 30 and 31 of the instant application add similar limitations with only minor differences, to independent claim 11 of the instant application that claims 2, 3, 4, 6, 7, and 8 of the copending application add to claim 1 of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1631

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LDR/

Larry Riggs

Examiner, Art Unit 1631

/Marjorie Moran/

Supervisory Patent Examiner, Art Unit 1631